AUSTRALIAN PATENT OFFICE

(B)

WRITTEN OPINION

	Date of mailing *day/month/year* 02 JUN 2003
Applicant's or agent's file reference 200130790/030423/TMSR/3220	**REPLY DUE** within FIVE MONTHS of the date of the Registrar's letter enclosing the written opinion

Application No.	Application Filing Date *(day/month/year)*	Priority Date *(day/month/year)*
SG 200103079-1	22 May 2001	17 July 2000

International Patent Classification (IPC) (as indicated in the search report)

Int. Cl.[7] C12Q 1/68

Applicant

WANG, XIAO BING et al

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1. This first written opinion consists of a total of 5 sheets.
2. This opinion contains indications relating to the following items:.
   - I [X] Basis of the opinion
   - II [ ] Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - III [ ] Lack of unity of invention
   - IV [X] Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - V [ ] Certain documents cited
   - VI [ ] Certain defects in the application
   - VII [X] Certain observations on the application
3. This opinion is based upon the assumption that the priority claim is valid.
4. The search report used was issued by the **Australian Office**, and the date of completion is: **28 May 2003**
5. If no reply is filed, the examination report will be established on the basis of this opinion.
6. The date by which the examination report will be established is: **17 October 2004**

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I. Basis of the opinion

1. This opinion has been drawn on the basis of:

[X] the application as originally filed.

[ ] the description, pages , as originally filed,
pages , filed with the request,
pages , received on with the letter of

[ ] the claims, pages , as originally filed,
pages , filed with the request,
pages , received on with the letter of

[ ] the drawings, sheets/fig. , as originally filed,
sheets/fig. , filed with the request,
sheets/fig. , received on with the letters of

[ ] the sequence listing part of the description:
pages , as originally filed
pages , filed with the demand
pages , received on with the letter of

2. The amendments have resulted in the cancellation of: pages:
sheets of drawings/figures No :

3 [ ] This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box.

4. Additional observations, if necessary:

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IV. Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims **19-22 and 28-30**	YES
	Claims **1-18, 23-27 and 31-36**	NO
Inventive step (IS)	Claims	YES
	Claims **1-36**	NO
Industrial applicability (IA)	Claims **1-36**	YES
	Claims	NO

2. Citations and explanations

The invention described in the specification resides in a method of detecting or quantifying a target nucleic acid sequence with respect to a specific base change in the sequence. The method broadly involves the use of primer that is complementary to the target sequence and that anneals to the target sequence immediately upstream of the specific base. Primer extension is then conducted using a mix comprising:
(i) one type of ddNTP, or an absence of the any nucleotide complementary to the specific base, and
(ii) the remaining three types of dNTPs that are different to the complement of the specific base, any of which may be optionally labelled.

Novelty and Inventive Step
The following documents identified in the International Search Report have been considered for the purposes of this report:

D1 WO 96 30545
D2 Braun et al
D3 US 5 888 819
D4 WO 91 13075
D5 Prezant et al
D6 Piggee et al

D1 discloses a method for detecting or quantifying a target nucleic acid sequence with respect to base changes at a specific location. In particular the method is used to assess mutations in the human COX1 gene, but it is also discloses that the method is suitable for a broad range of nucleic acids. D1 discloses use of a primer that whose 3' end is immediately adjacent to the base of interest. The primer is extended using a polymerase and a mix comprising one type of ddNTP, or an absence of nucleotide corresponding to the complement of the base of interest and from one to three of the remaining three types of nucleotide that are different to the complement of the specific base. The ddNTP and/or the dNTPs may optionally be labelled. As such the citation deprives claims 1-18, 23, 24, 27 and 31-36 of novelty.

With respect to the remaining claims, features such as those that enable attachment to a solid support, use of nucleotide analogues and extragenomic samples simply represent routine applications of the disclosed method that are standard in the art. As such these claims lack an inventive step.

Continued on supplemental sheet

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VII. Certain observations on the application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

[X] The claimed invention is patentable according to Section 13(2); or

[ ] The claimed invention is unpatentable according to Section 13(2) because:

Supplemental Box
(To be used when the space in any of Boxes I to VII is not sufficient)

Continuation of Box [No.]: IV2

D2 discloses a further method using a primer that anneals immediately adjacent to the base of interest and primer extension using a mix comprising the ddNTP corresponding to the complement of the base interest and three dNTPs that are different to the complement of the base of interest.. The method is used to assess mutations in the CFTR gene.

In particular figure 1(b) discloses the F508C mutation and the use of ddCTP as the chain terminator and 1(c) discloses the G542X mutation using ddTTP. The citation also discloses affinity capture of PCR products on solid phase and the use of modified nucleoside analogues. As such the citation deprives claims 1-6, 10-13, 23-27 and 31-36 of novelty.

Furthermore, as discussed with respect to D1, the subject matter of the remaining claims appears to represent nothing more than routine application of the method disclosed in the citation. As such, the remaining claims lack an inventive step in light of D2

D3-D6 all disclose similar methods to those disclosed in the specification. However D3 and D6 use only ddNTPs corresponding to the base of interest, with no added dNTPs and D4 and D5 disclose only dNTPS, with no added ddNTPs. As such none of D3-D6 appear to disclose or teach toward the subject matter of the claims.